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EXAMINER	
STRZELECKA, TERESA E	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 07/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/621,803	BROWNE, KENNETH A.	
	Examiner	Art Unit	
	Teresa E. Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,19,32,35 and 38-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,19,32,35 and 38-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to an amendment filed May 10, 2006. Claims 1-7, 9, 19 and 32-43 were previously pending. Applicant cancelled claims 33, 34, 36 and 37 and amended claims 1, 3-5, 7, 9, 19, 32, 35, 38 and 39. Claims 1-7, 9, 19, 32, 35, 38-43 are pending and will be examined. Applicant's amendments and arguments overcame the following rejections: rejection of claims 1-7, 9, 19 and 32-43 under 35 U.S.C. 112, first paragraph, written description; rejection of claims 1-7, 9, 19 and 32-43 under 35 U.S.C. 112, second paragraph; rejection of claims 1-7, 9, 32-35 and 37-42 under 35 U.S.C. 102(b) as anticipated by Brennan et al.; rejection of claim 19 under 35 U.S.C. 103(a) over Brennan et al., Hu et al. and Stratagene Catalog; rejection of claim 36 under 35 U.S.C. 103(a) over Brennan et al. and Lund et al.; rejection of claim 43 under 35 U.S.C. 103(a) over Brennan et al. and Gerard et al.

2. Applicant's arguments are moot in view of the new grounds for rejection presented below.

3. This office action contains new grounds for rejection necessitated by amendment.

Claim Interpretation

4. The term "surface" is interpreted as any area of the support.

5. Applicant did not define the term "species of probes" or "species of primer", therefore they are interpreted as either probes or primers with the same sequence within a species or as probes or primers with different sequences derived from the same target, for example.

6. Applicant defined the term "immobilized" with reference to a primer or probe on page 8, line 30, and page 9, lines 1-3, as follows:

"With reference to amplification primers, hybridization probes, or other compounds,

"immmobilized" is meant to convey that the compound joins, directly or indirectly, to a solid support. Immobilized compounds may be joined to the solid support by covalent or non-covalent interactions."

7. The limitations "no more than two species of labeled hybridization probes" and "no more than a single species of labeled hybridization probe" are interpreted as none, one or two species of probes and none or one species of probes, respectively.

8. The limitation "no more than a single species of amplification primer" is interpreted as none or a single species of the primer.

9. Applicant did not define the term "soluble primer", therefore any primer is considered to be "soluble".

10. The term "fluid communication" has been described by Applicant on page 9, lines 25-30 of the specification:

"As used herein, two molecules, such as an amplification primer and a hybridization detection probe, are said to be in "fluid communication" with each other when a third species, such as an amplicon, is able to freely interact with either or both of the two molecules. Two molecules that are in fluid communication with each other may, for example, be in the same well of a microplate with no physical barrier between the molecules."

11. The phrase "wherein each of said plurality of species of amplification primer and each of said plurality of species of labeled hybridization probes immobilized to said surface of said solid support is in fluid communication with the others" is interpreted as either the primer species being in fluid communication with each other, or the probe species being in fluid communication with each other or the primer species being in fluid communication with the probe species.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 32, 35 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 32 is indefinite over the recitation of "wherein said at least one species of labeled hybridization probe comprises no more than two species of labeled hybridization probe". There is an inconsistency in the claim, since "at least one" implies more than one, but "no more than two" means two, one or no probes.

B) Claims 35 and 38 are indefinite over the recitation of "wherein said at least one species of amplification primer comprises no more than a single species of amplification primer". There is an inconsistency in the claim, since "at least one" implies more than one, but "no more than one" means one or no probes.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1-6, 19, 32, 35, 38 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al. (U.S. Patent No. 6,060,288; cited in the IDS).

Regarding claim 1, Adams et al. teach a device for amplifying and detecting a target nucleic acid, the device comprising:

a solid support bead having a surface (Adams et al. teach a device for amplifying nucleic acids comprising beads (Fig. 1; col. 6, lines 65-67; col. 7, lines 41, 42).);

at least one species of amplification primer immobilized to said surface, said at least one species of amplification primer comprising a first amplification primer that comprises a sequence complementary to a first strand of said target nucleic acid (Adams et al. teach at least one species of primer immobilized to the beads, the primer being complementary to a target nucleic acid (Fig. 1; col. 2, lines 4-25; col. 3, lines 41-62).); and

at least one species of labeled hybridization probe immobilized to said surface,

wherein at least one of said at least one species of labeled hybridization probe comprises a sequence complementary to an amplicon synthesized using said first amplification primer and said target nucleic acid as a template in a nucleic acid amplification reaction, and

wherein each of said at least one labeled hybridization probe comprises a detectable label prior to contacting said device with any nucleotide polymerizing enzyme (Adams et al. teach detection of the amplicons with labeled hybridization probes (col. 4, lines 57-67); col. 13, lines 8-16). Therefore, since the probe is hybridized to an immobilized amplicon, the probe is itself immobilized, according to Applicant's definition. The probe is labeled independently of the polymerization reaction being performed.).

Regarding claim 2, Adams et al. teach glass and plastic (col. 7, lines 45-51; col. 14, lines 36-44).

Regarding claims 3-5, Adams et al. teach covalent immobilization of primers (col. 2, lines 1-3). Since the probes are attached to the primers, they are attached to the support, according to Applicant's definition.

Regarding claim 6, Adams et al. teach a second primer attached to the support, the primer complementary to the opposite strand from the first primer (col. 3, lines 41-46), therefore they teach soluble primers.

Regarding claim 19, Adams et al. teach a kit comprising solid supports with oligonucleotide primers attached (col. 6, lines 9-22), therefore, they teach soluble primers. Adams et al. teach positive controls (col. 5, lines 32-35).

Regarding claim 32, Adams et al. teach that each bead has primers which amplify a single target (col. 24, lines 20-67), therefore they inherently teach a single probe detection.

Regarding claims 35 and 38, Adams et al. teach that each bead has primers which amplify a single target (col. 24, lines 20-67), therefore teach a single species of the primers.

Regarding claim 39, Adams et al. teach that a composition comprising a device of claim 1, a pH buffer, a DNA polymerizing enzyme and dNTPs, where the probe and primer, or both primers, are in fluid communication with each other (Fig. 1; col. 9, lines 17-32; col. 10, lines 41-49; col. 13, lines 8-16).

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (U.S. Patent No. 6,060,288; cited in the IDS) and Whitcombe et al. (Nature Biotechn., vol. 17, pp. 804-807, 1999).

A) Adams et al. teach fluorescently labeled probes, but do not teach fluorophores and quenchers.

B) Whitcombe et al. teach amplification of target nucleic acids using primers which also serve as detection probes, where the probe part contains a fluorophore and a quencher (Fig. 1; page 804, paragraphs 5-7; page 805, first and second paragraphs).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the Scorpion primer of Whitcombe et al. in the amplification device of Adams et al. The motivation to do so, provided by Whitcombe et al., would have been, as stated by Whitcombe et al. (page 804, fourth paragraph):

"There are several consequences of this difference in probe–amplicon interaction. In particular, the appearance of signal is rapid and reliable, because probe–target binding is kinetically favored over duplex reannealing and thermodynamically favored over intrastrand secondary structures. The speed of these unimolecular binding events makes this signaling technology highly suitable for rapid assays in which equilibration times are short, giving it an advantage over bimolecular methods in which the rate of the PCR is reduced[14,15].", and (page 805, fourth and fifth paragraphs):

"The method works well for the detection of amplicon (Fig. 2A): large fluorescence increases were observed in the presence of amplicon, but not in the unamplified controls. Furthermore, the detection was highly specific, down to the level of single base changes. The use of stems in the probe element offers two advantages: first, background signals are minimal because signals from unincorporated Scorpions primers are switched off; second, the stem can be designed to be thermodynamically favored over the binding of probe to mismatch target. The allele-specific hybridization approach was extended to other allelic ratios, and we found that the magnitude of the allele-specific signal was proportional to the relative copy numbers of the variants (Fig. 2B).

The interaction between probe and target is efficient (see Fig. 3). Identical probe and amplicon sequences showed very different characteristics in a real-time assay. The bimolecular version of the assay did produce increased fluorescence, but the unimolecular version was much stronger (>20-fold)."

18. Claims 9 and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (U.S. Patent No. 6,060,288; cited in the IDS) and Mueller et al. (Histochem. Cell Biol., vol. 108, pp. 431–437, 1997; cited in the previous office action).

A) Adams et al. teach amplification of RNA targets (col. 8, lines 3-5), but do not teach amplification using primers comprising a promoter for RNA polymerase, T7 RNA polymerase or reverse transcriptase.

B) Mueller et al. teach amplification of RNA targets using a self-sustained sequence replication method (3SR), which uses a primer containing a T7 polymerase promoter, T7 RNA polymerase and AMV reverse transcriptase (Fig. 1; page 432, third paragraph). Mueller et al. teach ribonucleotide phosphates (page 435, Table 3).

It would have been *prima facie* obvious to one of ordinary skill in the art to have used the 3SR reagents of Mueller et al. in the device of Adams et al. The motivation to do, provided by Mueller et al., would have been, as stated on page 432, last paragraph and page 433, first and second paragraphs:

"Despite its complexity at the molecular level, the 3SR reaction is simple to perform since all enzymes can be added in a single step to a single reaction mixture at a constant temperature. There is no need for a thermocycler or for heat stable enzymes and, since there are no denaturing conditions, there is no need to add fresh enzymes. (For additional comments comparing PCR to 3SR see Lown 1993.)

Regarding reaction kinetics, the rate of amplification with 3SR is extremely fast in comparison to PCR, especially in the early phases of the reaction. HIV viral RNA has been found to multiply 12 copies to 1010 copies in 90 min by in vitro 3SR (Bush et al. 1992). Another study showed that, while PCR required 85 min to amplify a template 105 times, 3SR can reach the same level of amplification in 15 min (Guatelli et al. 1990). This rapid rate of amplification means that the incubation time for the 3SR reaction can be quite short, usually only 1–2 h."

19. Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (U.S. Patent No. 6,060,288; cited in the IDS) and Mueller et al. (Histochem. Cell Biol., vol. 108, pp. 431–437, 1997; cited in the previous office action) as applied to claim 42 above, and further in view of Gerard et al. (Mol. Biotech., vol. 8, pp. 61-77, 1997; cited in the previous office action).

A) Claim 43 is drawn to the method of claim 42 where the reverse transcriptase is an MMLV reverse transcriptase. The teachings of Adams et al. and Mueller et al. are presented above. Mueller et al. teach reverse transcriptase, but do not specifically teach an MMLV reverse transcriptase.

B) Gerard et al. teach DNA polymerization using an MMLV reverse transcriptase without RNAse H activity (Abstract; page 62, first paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the MMLV reverse transcriptase of Gerard et al. in the liquid composition of Adams et al. and Mueller et al. The motivation to do so, provided by Gerard et al., would have been that MMLV without RNASe H activity synthesized cDNA more efficiently (Abstract).

20. No claims are allowed.

Conclusion

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
Primary Examiner
Art Unit 1637

Teresa Strzelecka
7/19/06